2014-1139, -1144

United States Court of Appeals for the Federal Circuit

ARIOSA DIAGNOSTICS, INC., and NATERA, INC.,
Plaintiffs-Appellees,

and

DNA DIAGNOSTICS CENTER, INC.,
Counterclaim Defendant-Appellee,

v.

SEQUENOM, INC., and
SEQUENOM CENTER FOR MOLECULAR MEDICINE, LLC,
Defendants-Appellants,

and

ISIS INNOVATION LIMITED,
Defendant.

Appeals from the United States District Court for the Northern District of California in Nos. 3:11-cv-06391-SI, and 3:12-cv-00132-SI, Judge Susan Y. Illston.

THE BIOTECHNOLOGY INDUSTRY ORGANIZATION (BIO) AND PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA (PhRMA) AS *AMICI CURIAE* SUPPORTING APPELLANTS AND IN FAVOR OF EN BANC RECONSIDERATION

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August 27, 2015

CERTIFICATE OF INTEREST

Counsel for *Amici Curiae* certifies the following:

1. The full name of every party or *amicus curiae* represented by me is:

   Biotechnology Industry Organization ("BIO")
   Pharmaceutical Research and Manufacturers of America ("PhRMA")

2. The name of the real parties in interest (if the party named in the caption is not the real party in interest) represented by me is:

   None.

3. All parent corporations and any publicly held companies that own 10 percent of the stock of the party or *amicus curiae* represented by me are:

   None.

4. The names of all law firms and the partners or associates that appeared for the party or *amici curiae* now represented by me in the trial court or are expected to appear in this court are:

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STATEMENT OF INTEREST OF AMICI CURIAE

The Biotechnology Industry Organization (BIO) is the world's largest biotechnology trade association, with over 1,100 members worldwide involved in the research and development of innovative healthcare, agricultural, industrial, and environmental biotechnology products. The Pharmaceutical Research and Manufacturers of America (PhRMA) is a voluntary, nonprofit association representing the nation's leading research-based pharmaceutical and biotechnology companies. PhRMA's member companies are dedicated to discovering medicines that enable patients to lead longer, healthier, and more productive lives. BIO and PhRMA are concerned that the development and commercialization of a range of biotechnologies will be impeded if this Court does not address the mounting uncertainty currently afflicting patentable subject matter jurisprudence.

Amici have no direct stake in the result of this appeal. No counsel for a party authored this brief in whole or in part, and no such counsel or party, nor any person other than the amici curiae or their counsel, made a monetary contribution intended to fund the preparation or submission of this brief. This brief is solely the work of BIO and PhRMA and their counsel; it reflects the amici's consensus view, but not necessarily the view of any individual member. Pursuant to Fed. Cir. R. 35(g) amici are contemporaneously filing a motion for leave to file this brief.

ARGUMENT

I. The Panel Decision Has Exacerbated Uncertainty as to the Availability of Effective Patent Protection for Biotechnological Innovation

The rapid expansion of biotechnology beginning in the 1980s has been attributed, at least in part, to the inclusive scope of patentable subject matter espoused by the Supreme Court in *Diamond v. Chakrabarty*, 447 U.S. 303 (1980). Unfortunately, recent rulings have resulted in a level of uncertainty about the scope of patent-eligible subject matter that is unprecedented in the history of biotechnology. This is affecting both the patent user community and the US Patent and Trademark Office (PTO), which has responded with an ongoing stream of revised and re-revised non-final and interim guidance documents. With each new PTO guidance, biotech companies have observed an increasing rate of claim rejections, affecting a diverse range of biotechnology, including novel antibiotic molecules, industrial enzymes, diagnostic processes, and crop protection products, to name but a few.[1]

Until recently, such inventions were uncontroversially deemed patent eligible, and still are in other industrialized countries, where trading partners are growing concerned about a widening U.S. departure from internationally prevailing standards for patent eligibility of at least some biotechnologies, and its

[1] See e.g. Chao, Bernard, *The USPTO Is Rejecting Potentially Life-Saving Inventions;* available at http://www.law360.com/articles/604808/uspto-is-rejecting-potentially-life-saving-inventions.

effect on trade and the cross-border flow of innovation and investment.[2]

Even if a biotechnology firm succeeds in overcoming a rejection on patent-eligibility grounds in the PTO, the unsettled state of the law creates doubt about whether such issued patents would withstand challenge. So far, the vast majority of judicial decisions addressing patent eligibility across technologies have resulted in a determination of ineligibility under the recently articulated standards. For example, Appendix 3 of the the recent PTO "July 2015 Update: Subject Matter Eligibility," identifies 24 post-*Mayo* subject matter eligibility decisions of this Court alone.[3] Of these, 22 held *all* of the challenged claims to be patent ineligible.

The dark cloud overshadowing thousands of issued and maintained biotechnology patents,[4] many of which have been the basis for substantial investment, threatens investors' expectations that appeared reasonable prior to recent jurisprudential developments. And the resulting uncertainty is affecting future investment decisions. Biotechnology is often identified as one of the areas of technology most dependent upon effective and predictable patent protection, in the

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[2] See 2014 and 2015 Comments of International Bioindustry Associations, available at http://www.uspto.gov/sites/default/files/patents/law/comments/mm-a-bio20140731.pdf and http://www.uspto.gov/sites/default/files/documents/2014ig_a_bio_2015mar16.pdf , respectively.

[3] Available at http://www.uspto.gov/patent/laws-and-regulations/examination-policy/examination-guidance-and-training-materials.

[4] For example, the *Myriad* decision alone effectively invalidated isolated nucleic acid claims in over 8,700 issued and maintained US patents - this effect is much greater when extrapolated to claims to other isolated naturally-occurring substances. See Graff, Gregory D. et al., *Not quite a myriad of gene patents*, Nature Biotechnology 31(5) (2013) 404-410.

absence of which investors will choose to switch to other, perhaps less socially beneficial, areas of technology. *In re Bilski*, 545 F.3d 943, 1014 (Fed. Cir. 2008) (J. Rader, dissenting) (warning of the danger of "inadvertently advis[ing] investors that they should divert their unprotectable investments away from discovery of 'scientific relationships' within the body that diagnose breast cancer or Lou Gehrig's disease or Parkinson's [ ].").

II. This Court Should Clarify the Contours of the *Mayo* Framework

Mayo established a two-step framework, inquiring first whether the claims at issue are "directed to" excluded subject matter, and, if so, asking second, whether the claim nonetheless embodies an "inventive concept." *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371, 1375 (Fed. Cir. 2015)(citing *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 132 S.Ct. 1289, 1297).

Clearly, the Supreme Court would not have articulated a two-step test if it did not intend the first step to serve a meaningful gatekeeping function. Yet, the panel missed an opportunity to clarify if and how this gatekeeping function operates in biotechnology. For example, the panel indicates that a claim "directed to detecting the presence of a naturally occurring thing or natural phenomenon" meets Step I. But under this logic, it is difficult to see how *any* analytical or detection method would ever *not* satisfy Step I, so long as that method is designed to detect something that occurs naturally. Such uncritical application of Step I would render the first part of the Supreme Court's test superfluous for a vast array

of technologies, including not only virtually all diagnostics, but also forensic, geological or atmospheric testing, petrochemical or metallurgical analysis, and even radioisotope dating in archaeology. The panel's analysis would also promote disparate treatment of analytical methods based on what these methods detect, even if they are otherwise indistinguishable from a practical and social utility perspective. For example, a method for detecting man-made toxic contaminants in drinking water might be found patent eligible under Step I, while a functionally equivalent method for detecting waterborne natural pathogens would advance to higher scrutiny under Step II.

Whether or not Step I plays a meaningful gatekeeping role also has serious implications for personalized medicine, widely heralded as the next generation of medical innovation. Personalized medicine inventions inherently rely on the detection or evaluation of a patient-specific trait, or on a patient's physiological response to a treatment, and could categorically be deemed "directed to" a natural phenomenon under an uncritical or undifferentiated application of Step I. It seems unlikely this was the intent of the Supreme Court, and *en banc* reconsideration could provide an opportunity to clarify the contours of Step I of the *Mayo* framework in the context of personalized medicine, and biotechnology in general.

There is also a great need for *en banc* clarification of the parameters of Step II of the *Mayo* analysis. One particular area of confusion concerns the interplay of analysis for "inventive concept" and "preemption." Often, the existence of

preemption and inventive concept are not connected, and in fact threaten to drive the development of patent eligibility doctrine in different directions. For example, an application of a biological natural phenomenon that is highly inventive might constitute the only practical use of the phenomenon apparent at the time of invention. Should its patent-eligibility be upheld because of the presence of an inventive concept, or barred because of its apparent preemption of the natural phenomenon? On the other hand, it will always be possible to limit a claim by including conventional steps, such that the public retains virtually unfettered access to the implicated natural phenomenon. Does a manifest lack of preemption ever remove the need for an "inventive concept" analysis, or influence it in any way?

The panel's interpretation of the "inventive concept" test is likewise problematic. It will often be the case that an otherwise novel and nonobvious biotechnology invention can be deconstructed into a mere combination of natural phenomena and known techniques. But biotechnology has advanced through inventions of this type, which prior to the recent Supreme Court decisions have been viewed as eligible for patent protection. Such inventions translate nascent technology into commercial products that provide meaningful benefits to society. Patents on diagnostics, for example, play a critical role as the necessary incentive for the substantial investment required for commercialization activities such as clinical studies in support of regulatory approval, insurance reimbursement, and

even the necessary studies to ensure healthcare providers and patients have sufficient information to avail themselves of the technology.[5]

The basis for innovation in genetic diagnostic testing is the identification of a genetic variation that correlates with some clinically significant information regarding a patient, such as a propensity for cancer, or the optimal dosage of a drug.[6] These are extremely important innovations, but the resulting clinical tests generally involve the use of conventional techniques for amplifying and analyzing DNA, such as polymerase chain reaction (PCR) and electrophoresis (the techniques used in this case). Because such techniques are well-understood, validated, and reliable, their use for medical applications makes good sense. Yet if the genetic variation is characterized as a natural phenomenon, as seems likely under recent jurisprudence, the reasoning applied by the panel could generally preclude patent eligibility for diagnostic tests simply because the most practical means for administering the tests involves the use of conventional techniques.

In its recent decisions the Supreme Court apparently assumed the existence of limiting principles that would maintain patent eligibility for truly meritorious inventions (Judge Linn's characterization of the claims at issue in this case), even

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[5] See e.g. Holman, Christopher M., *The Critical Role of Patents in the Development, Commercialization and Utilization of Innovative Genetic Diagnostic Tests and Personalized Medicine* (2014) , available at http://cpip.gmu.edu/wp-content/uploads/2014/04/Holman-Critical-Role-of-Patents-in-Genetic-Diagnostic-Tests.pdf.

[6] *Id.*

if that invention can be deconstructed into a combination of natural phenomena and conventional technology. *Mayo*, for example, reaffirmed the continuing viability of *Diamond v. Diehr*, a decision in which the Court upheld the patent eligibility of a process comprising an inventive application of a mathematical equation implemented by means that would appear to have been conventional and routine at the time of invention. 132 S.Ct. at 1299 (citing *Diamond v. Diehr*, 450 U.S. 175 (1981). *Mayo* found that the *Diehr* claim did satisfy the "inventive concept" test because these steps "apparently added to the formula something that in terms of patent law's objectives had [significance, transforming] the process into an inventive application of the formula." *Id.* Note *Mayo*'s focus on the *objectives* of patent law - which would clearly encompass providing adequate patent protection for meritorious inventions - and its conclusion that when these objectives are satisfied, a claim reciting the application of an excluded law of nature with conventional and well-known process steps can be patent eligible. *Diehr* also emphasized that the claims deemed patent eligible in that case did "not seek to pre-empt the use of [the mathematical] equation," an important consideration that was given short shrift by the panel in this case.

En banc reconsideration would allow this court to address the nature of the limiting principles suggested in *Mayo*. Alternatively, if this court finds that Supreme Court precedent does not provide for limiting principles that provide a meaningful opportunity for patenting important biotechnology innovations, that

would suggest a need for the Supreme Court to readdress the contours of patent eligibility in the context of biotechnology. This case would be an appropriate vehicle to alert the Supreme Court to the urgent need for this clarification.

Some opinions seem to suggest that the developer of, for example, a new diagnostic test can avoid subject matter eligibility problems by coming up with some new methodology for analyzing DNA, enzymes or other patient-specific traits, and then patenting a method limited to this new methodology. But this is not a realistic proposal. The resulting patent claim would have little commercial value, since it would permit competitors to perform equivalent diagnostic tests using conventional methodology without any liability. An informed consideration of the practicalities of personalized medicine suggests that the Federal Circuit must begin articulating limiting principles in order to achieve the Supreme Court's objective of balancing access to the building blocks of innovation against reasonable scope of patent protection for important inventions in the life sciences.

III. A Coherent Articulation of the Policy Basis for the Patent Eligibility Requirement is Necessary for Development of the Doctrine in a Manner Consistent with the Overarching Objectives of the Patent System

Nothing in *Mayo* and *Myriad* suggests that the Court intended to single out whole classes of socially beneficial biotechnology for unfavorable treatment under the patent law - to the contrary, these decisions are replete with cautionary statements indicating that the Court did not envision its decisions as upsetting the availability of effective patent protection for biotechnology inventions, particularly

in the areas of diagnostics and pharmaceuticals. We are reminded that the statute is inclusive and judicial exceptions to it are narrow, not the other way round.

For example, in *Myriad* the Court stressed that its decision did not implicate "patents on new *applications* of knowledge about the BRCA1 and BRCA2 genes." *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107, 2120 (2013). To the contrary, the Court assumed that effective patent protection would remain available for those who discovered new information useful for the development of diagnostic tests. *Myriad* quotes approvingly from the panel decision below, where Judge Bryson had "aptly noted that, '[a]s the first party with knowledge of the [BRCA1 and BRCA2] sequences, Myriad was in an excellent position to claim applications of that knowledge. Many of its unchallenged claims are limited to such applications." *Id.* (citing *Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office*, 689 F.3d 1303, 1349 (Fed. Cir. 2012).

Two years later, the patent user community is left to wonder which claims those might be. Claims identified by Judge Bryson, which the Supreme Court assumed to be available to Myriad, were subsequently declared patent ineligible by the Federal Circuit for failure to satisfy the *Mayo* framework. *University of Utah Research Foundation v. Ambry Genetics Corp*., 774 F.3d 755 (Fed. Cir. 2014).

CONCLUSION

For these reasons, this Court should grant en banc reconsideration of this case.

Respectfully submitted,

Date: August 27, 2015

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CERTIFICATE OF SERVICE

I, Robyn Cocho, being duly sworn according to law and being over the age of 18, upon my oath depose and say that:

Counsel Press was retained by Hovey Williams LLP, counsel for Amici Curiae, BIOTECHNOLOGY INDUSTRY ORGANIZATION and PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA, to print this document. I am an employee of Counsel Press.

On **August 27, 2015**, Counsel for *Amici Curiae* has authorized me to electronically file the foregoing **Brief of *Amici Curiae*** with the Clerk of Court using the CM/ECF System, which will serve via e-mail notice of such filing to any of the following counsel registered as CM/ECF users:

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Any counsel for Amici Curiae who are registered users, at the time of filing, will also be served via e-mail notice from the Clerk of Court via the CM/ECF System.

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August 27, 2015

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